Endothelial progenitor cell dysfunction: is it best fitted for risk stratification in pulmonary disease?

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ABSTRACT

Endothelial progenitor cell (EPC) dysfunction is defined as weak function and lowered number of endothelial precursors with pro-angiogenic phenotypes that are imbedded in vascular integrity maintenance, angiogenesis, and vascular reparation. There is large body of evidence that deficiency of EPC number in peripheral blood is considered as a marker of endothelial dysfunction, which is established risk factor and player in pathogenesis of cardiovascular disease. Moreover, recent clinical studies have shown that circulating EPCs had demonstrated vascular protection in several vascular diseases including pulmonary hypertension. However, the role of EPCs in pathogenesis chronic obstructive pulmonary disease bronchial asthma, emphysema appeared to be uncertain. The short communication is dedicated the controversies in abilities of EPCs to have tissue protective and play a pivotal role in nature evolution of pulmonary disease.

Keywords: pulmonary disease, cardiovascular risk, endothelial dysfunction, endothelial precursors, prediction, prognosis
1. INTRODUCTION

Endothelial progenitor cells (EPCs) are defined as various populations of primitive CD34+ endothelial precursors with different origin that additionally express CD31, CD133, CD144 and VEGFR2 antigens [1]. Although previous investigations, which had seized molecular characteristics of EPCs, have sufficiently been distinguished in hierarchy, colony-forming and proliferation capacities, as well as immune phenotypes [2, 3], the most specific property of these cells remained an ability to be a source for renewal of mature endothelial cells [4]. Thus, EPCs are determined as a component of endogenous vascular repair system that supports vascular integrity, endothelial function, angiogenesis, neovascularization and reparation [5].

There is a large of body evidence that decreased number and / or weak function of EPCs known as EPC dysfunction frequently proceeded to developing cardiovascular (CV) disease and / or CV events and also accompanied CV risk factors [6-8]. Indeed, declined number of circulating EPCs was associated with CV complications, but restoring of a pole of angiopoetic endothelial precursors was related to an attenuation of vascular function, decreasing of a risk of CV events and improving of clinical outcomes [9, 10]. It has been suggesting that EPCs were not just able to produce wild range of spectrum of angiopoetic factors contributing in the angiogenesis and vascularization (hormones, microRNAs, growth factors, active peptides and molecules), but they are directly imbedded in the differentiation into mature endothelial cells and smooth muscle cells of vascular wall supporting vascular integrity and function [11].

The regulation of autocrine EPC function is performed through several signal systems (Akt, nuclear factor-kappa B; STAT, and Notch signaling) and epigenetically via target genes (hey1, hes1, cdkn1c and il33) that mediate an activity of intracellular signal systems [12]. Key triggers for EPC activity were pro-inflammatory cytokines (tumor necrosis factor-alpha, interleukin-6), growth factors (vascular endothelial growth factor, transforming growth factor-beta, hypoxia inducible factor-1), hormones (angiotensin-II, renin, and endothelin-1), and oxidative stress components (oxidized lipids) [13].

EPCs are implicated in the pathogenesis of numerous respiratory diseases, including chronic obstructive pulmonary disease (COPD) and emphysema and correspond to CV risk in the diseases [11, 14]. It is well known that mobbing and differentiation of EPCs mediate airway wall neovascularisation, which is a prominent feature of COPD, is associated with reticular basement membrane thickening and airway obstruction [15]. Additionally, sub-epithelial vascularization in COPD may be an important remodeling event for airway narrowing and airflow obstruction. On the other hand, deficiency of EPCs corresponded to endothelial dysfunction, which is core element on pathogenesis of pulmonary hypertension in COPD and emphysema patients. In this context, EPCs may play controversial role in COPD nature evolution. The results of the Multi-Ethnic Study of Atherosclerosis COPD Study recruited smokers with age from 50 years to 79 years without clinical CV disease revealed that populations of pro-angiogenic EPCs with immune phenotypes CD34+VEGFR+ and CD34+VEGFR+CD133+ cells were significantly reduced in COPD and emphysema patients in comparison with healthy volunteers.

Moreover, number of circulating CD34+VEGFR+CD133+ EPCs was associated inversely to severity of emphysema [16], was not related to COPD severity [17]. Noted there was not significant difference between number of circulating EPCs in smokers and nonsmokers [18]. Additionally, number of EPCs in peripheral blood predicted cardiac dysfunction due to
COPD and strong associated with morbidity in patients with acute exacerbation of COPD [19]. There is point of view that chronic inflammation that is suitable for COPD does not impact only on bronchial wall and lung parenchyma, buy yet it potentially exists as systemic phenomenon, which reduces vasodilatation capacity, enhanced blood coagulation, and increased platelet activation resulting in higher risk of CV complications [20, 21].

Thus, EPCs plays positive role in supporting vascular integrity and function, but they influence negatively on bronchial remodeling. On contrary, there is evidence that EPCs are able to attenuate developing pulmonary emphysema and improve of lung function by alleviating inflammatory infiltration in alveoli, decelerating apoptosis of alveolocytes, inhibiting proteolytic enzyme activity, and improving antioxidant defense [22, 23]. Finally, these findings require to be investigated in details in large clinical trials in the future.

2. CONCLUSIONS

In conclusion, EPCs may play a duel role in the pathogenesis of pulmonary disease. On the one hand, they contribute vascular repair, support endothelial function and maintain lung homeostasis. On the other hand, angiogenesis in sub-intima of bronchial wall provide reticular basement membrane thickening and lead to airway obstruction. Both abilities of EPC subsets expressed angiogenesis-related molecules require to be accurate identified and compared each other in clinical studies affecting several populations of the patients with established pulmonary diseases.

References


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